REMARKS

Claim 39 has been amended to incorporate the limitations from Claim 40. Claim 41 has been amended to correct claim dependency. Claims 51, 63, and 68 have been amended to recite ophthalmic administration and to clarify the claim language. Claims 35-36, 40, 49, 57-62, 76-121, 126, 131, and 133 have been canceled without prejudice to pursuing them in a divisional, continuation, or continuation-in-part application. Claims 76-121 are being pursued in a divisional application filed on even date herewith. Claims 30-34, 37-39, 41-48, 50-56, 63-75, 122-125, 127-130, 132, and 134 remain pending. Claims 75, 122-125, 127-130, 132, and 134 have been withdrawn.

The Applicants have carefully considered all of the Examiner's rejections but respectfully submit that the claims are allowable for at least the following reasons.

Withdrawn Claims

The Examiner withdrew Claims 75-134 from consideration for allegedly being directed to non-elected subject matter. Applicants respectfully traverse the withdrawal with respect to Claims 75, 122-125, 127-130, 132, and 134. In their April 10, 2007 election of species, Applicants elected "rapamycin and analogs and derivatives thereof" and "wet form of age-related macular degeneration." As stated in their election, then pending Claims 30-75 encompassed these species. In the July 6, 2007 Office Action, the Examiner examined Claim 75, which depends from Claim 68. Thus, the Examiner has already recognized that Claim 75 is directed to the elected subject matter and Applicants respectfully request that Claim 75 be restored to non-withdrawn status.

Claims 122-125, 127-130, 132, and 134 depend from examined Claims 30, 38, 39, 43, 51, 57, or 63 and are directed to and read on the elected species. Accordingly, Applicants respectfully request that Claims 122-125, 127-130, 132, and 134 also be examined.

Rejections under § 112 – Enablement

Claims 57-62 stand rejected under 35 U.S.C. § 112, first paragraph, allegedly because the specification, while being enabling for the treatment of macular degeneration, does not reasonably provide enablement for preventing wet form macular degeneration. Although Applicants respectfully traverse this rejection, Applicants hereby cancel Claims 57-62, in order to further the prosecution of the present application and Applicants' business interest, without

acquiescing the Examiner's arguments, while reserving the right to prosecute the original, similar or broader claims in one or more future application(s). Cancellation of the rejected claims hereby renders this rejection moot.

Rejections under § 102

Claims 30-74 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Mollison (U.S. Patent No. 6,015,815). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 621, 631 (Fed. Cir. 1987)). "The identical invention must be shown in as complete detail as is contained in the ... claim." M.P.E.P. § 2131 (quoting *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989)). "The elements must be arranged as required by the claim." M.P.E.P. § 2131 (citing *In re Bond*, 910 F.2d 831 (Fed. Cir. 1990)). Applicants respectfully submit that Mollison does not disclose each element of every claim as detailed below.

Claims 30-34, 37-38, and 42-43

Independent Claim 30 recites a composition comprising rapamycin and polyethylene glycol. Independent Claim 38 recites a composition comprising rapamycin dissolved in polyethylene glycol and ethanol. Mollison does not disclose such compositions. Rapamycin is disclosed in the "Background of the Invention" section as a previously known anti-fungal, antitumor, and immunosuppressant agent. *See* Mollison, column 1, line 63 to column 2, line 41. The "Background" section of Mollison concludes that "the need remains for macrocyclic immunosuppressants which do not have the serious side effects frequently associated with immunosuppressant therapy due, in part, to the extended half lives of the immunosupressants." Column 3, lines 17-22. Mollison goes on to disclose the novel compounds of the invention, which ***do not include rapamycin***. *See* column 3, lines 35-55.

That the compounds of Mollison do not include rapamycin is further demonstrated by the fact that "the compounds of the present invention was [sic] compared to rapamycin." Mollison, column 7, lines 33-34. It was found that the compounds of the invention "had a surprisingly substantially shorter terminal elimination half-life ($t_{1/2}$) when compared to rapamycin." Column 8, lines 35-36. Mollison concludes that, compared to rapamycin, "only the compounds of the invention provide both sufficient efficacy (Table 1) and a shorter terminal half-life (Table 2)."

Column 8, lines 37-38. Thus, Mollison teaches that rapamycin is not a compound of the invention and therefore, all of the compositions and methods disclosed in Mollison do not apply to rapamycin.

Specifically, the disclosure in Mollison regarding "pharmaceutical compositions" pertain to "***a compound of the invention*** and a pharmaceutically acceptable carrier or excipient." Column 11, lines 49-51. Thus, the disclosure in Mollison of polyethylene glycol in a composition for parenteral injection (column 12, lines 4-5) and in a liquid oral dosage form (column 13, line 35) ***does not include rapamycin***.

The Examiner may not take the disclosure of rapamycin in the "Background" section of Mollison out of context and combine it with the excipients disclosed for use with the "compounds of the invention." The instant case is closely analogous to *Ecolochem Inc. v. Southern California Edison Co.*, 56 U.S.P.Q.2d 1065 (Fed. Cir. 2000). In *Ecolochem*, the patentee had claims directed to a deoxygenation process that involved using hydrazine among other process steps. 56 U.S.P.Q.2d at 1067. The district court had found that the claims were anticipated by the Martinola articles. The Martinola articles noted that the use of hydrazine in water deoxygenation "had been in use, but that the chemical process of deoxygenating water with hydrogen had not been, and conclude[d] that the hydrogen process is preferable." *Id.* at 1069. The authors of the articles concluded that "[i]f we compare the final costs ... we find that the method of oxygen reduction with hydrogen is much cheaper than the other methods." *Id.* at 1070. The articles go on to present a "Figure 10" which disclosed other elements of the claims. *See id.* at 1069. The Federal Circuit concluded that "Figure 10" of the Martinola articles only pertained to the use of hydrogen and not the use of hydrazine, despite the fact that hydrazine was disclosed in the articles as discussed above. *See id.* at 1069-1070. The Federal Circuit found that the textual discussion in the articles implied that the processes described in "Figure 10" were intended to be used with the hydrogen method and not the prior hydrazine method that the authors found to be inferior. *See id.*

Similarly, in the instant case, Mollison only discuses rapamycin in the context of being a previously known compound inferior to the "compounds of the invention." The disclosure in Mollison regarding pharmaceutical compositions pertain to the "compounds of the invention" and not rapamycin. Thus, Applicants respectfully submit that Mollison does not disclose a

composition comprising rapamycin and polyethylene glycol and therefore, does not anticipate Claim 30. Dependent Claims 31-34 and 37 are similarly not anticipated. Mollison also does not disclose a composition comprising rapamycin dissolved in polyethylene glycol and ethanol and therefore, does not anticipate Claim 38. In addition, Claims 42-43, which depend from Claim 39 (discussed below), recite a composition comprising rapamycin, tacrolimus, everolimus, pimecrolimus, SDZ-RAD, CCI-779, AP23841, or ABT-578. None of these compounds are the "compounds of the invention" in Mollison. Accordingly, Mollison also does not anticipate Claims 42-43.

In addition, Claims 30 and 38 recite a composition suitable for ophthalmic administration by injection. The only instance in which ophthalmic administration is mentioned in the disclosure of Mollison is in connection to methods of topical administration. Mollison teaches that "[t]opical administration includes administration to the ... eye," and that "the compound is maintained in contact with the ocular surface for a sufficient time period to allow the compound to penetrate the corneal and internal regions of the eye." Mollison, column 13, lines 46 and 47, and column 14, lines 9-12. Accordingly, since topical administration to the eye is distinct from "ophthalmic administration by injection," Mollison fails to teach the mode of administration of Claims 30 and 38, regardless of whether the compositions of Mollison comprise PEG.

Furthermore, the only instance in which PEG is mentioned in the disclosure of Mollison is in connection with compositions for parenteral injection, oral administration, rectal administration and vaginal administration (Mollison, column 11, line s 4 and 5, column 13, line 3 and line 35, and column 14, line 22). Mollison goes on to teach that the "term 'parenteral,' as used herein, refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion" (Mollison, column 11, lines 59-63). Accordingly, since parenteral injection, oral administration, rectal administration and vaginal administration as defined by Mollison clearly do not encompass topical administration as taught by Mollison, this single reference does not provide the requisite teaching or suggestion to include PEG in ophthalmic formulations.

Thus, for the additional reason that the ophthalmic compositions of the cited art (Mollison) do not comprise PEG as recited in Claims 30 and 38, Applicants respectfully submit that Claims 30-34 and 37-38 are not anticipated.

Claims 39-50

Independent Claim 39 recites an ocular composition comprising polyethylene glycol that is suitable for ophthalmic administration by injection. Mollison does not disclose such a composition. As discussed above, the only compositions disclosed in Mollison that comprise polyethylene glycol are those for parenteral injection (*see* column 11, line 64 to column 12, line 5) and an oral liquid dosage form (*see* column 13, lines 24-35). As noted above, anticipation requires that "[t]he identical invention must be shown in as complete detail as is contained in the ... claim." M.P.E.P. § 2131 (quoting *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989)). "The elements must be arranged as required by the claim." M.P.E.P. § 2131 (citing *In re Bond*, 910 F.2d 831 (Fed. Cir. 1990)). Mollison simply does not disclose use of polyethylene glycol in an ocular composition that is suitable for ophthalmic administration by injection. Accordingly, Applicants respectfully submit that Claim 39 is not anticipated by Mollision. Similarly, dependent Claims 40-50 are not anticipated for at least the same reasons.

Claims 51-56

Independent Claim 51 recites a method of treating a human having the wet form of age-related macular degeneration by administering rapamycin dissolved in polyethylene glycol. As discussed above, Mollison does not disclose rapamycin dissolved in polyethylene glycol and this reason alone is sufficient to overcome the anticipation rejection of Claims 51-56. In addition, Mollison does not disclose the use of rapamycin to treat the wet form of age-related macular degeneration. In discussing "Methods of Treatment," Mollison refers to "[t]he compounds of the invention." *See* column 8, line 52 and column 9, lines 25-26. As discussed above, these compounds do not include rapamycin. Thus, none of the listed diseases, including "senile macular degeneration" (column 9, line 66), are disclosed as being treatable by rapamycin. Furthermore, "senile macular degeneration" is included in a list of "[o]ther treatable conditions" (column 9, line 26) and not as a disease related to the immunosuppressant activity possessed in common by the "compounds of the invention" and rapamycin. *See* Mollison, column 8, lines 54-66 (listing diseases associated with immunosuppressant activity, which does not include senile

macular degeneration). As in the *Ecolochem* case discussed above, the text of Mollison indicates that the recitation of "senile macular degeneration" pertains to the "compounds of the invention" and not rapamycin. *See also Merck & Co. v. Teva Pharmaceuticals USA Inc.*, 68 U.S.PQ.2d 1857, 1861 (Fed. Cir. 2003) (holding that a method-of-treatment claim was not anticipated by prior art disclosing the claimed compound as being useful for pharmaceutical preparations but not disclosing that the compound was useful for the specifically claimed indication and stating that "[a]n 'anticipating' reference must describe all of the elements and limitations of the claim in a single reference, and enable one of skill in the field of the invention to make and use the claimed invention."). Finally, the disclosure of "senile macular degeneration" in Mollison is not a specific disclosure of the wet form of age-related macular degeneration. As discussed in the instant specification, age-related macular degeneration exists in two forms: the dry form and the wet form. Mollison does not identify treatment of the wet form.

For any of the above reasons, Applicants respectfully submit that Claim 51 is not anticipated by Mollison. Dependent Claims 52-56 are similarly not anticipated. Furthermore, Claims 52-56 recite specific ocular administration techniques not disclosed by Mollison. Mollison discloses nothing about placing a composition into the vitreous (Claim 52), intravitreal injection (Claim 53), placement between the conjuctiva and the sclera (Claim 54), or subconjunctival injection (Claim 55). Instead, as discussed above, Mollison only discloses "topical administration ... to the eye" by contacting compounds "with the ocular surface." Column 14, lines 4-10. For this additional reason, Claims 52-56 are not anticipated by Mollison.

Claims 63-67

Independent Claim 63 recites inhibiting the transition in a human from the dry form of age-related macular degeneration to the wet form by administering rapamycin dissolved in polyethylene glycol. For at least the reasons discussed above regarding the failure of Mollison to disclose rapamycin dissolved in polyethylene or the use of rapamycin to treat macular degeneration, Applicants respectfully submit that Claims 63-67 are not anticipated. In addition, Mollison is silent regarding the dry and wet forms of macular degeneration, let alone inhibiting the transition from the dry form to the wet form. Thus, for this additional reason, Applicants respectfully submit that Claim 63 and dependent Claims 64-67 are not anticipated by Mollison. Furthermore, as discussed above with respect to Claims 52-56, Mollison fails to disclose the

specific ocular administration techniques recited in dependent Claims 64-67. For this additional reason, Claims 64-67 are not anticipated by Mollison.

Claims 68-74

Independent Claim 68 recites treating an angiogenesis-mediated disease or condition of the retina or choroid using a composition of Claims 30 or 39. Thus, Claims 68-74 are not anticipated for at least the same reasons as Claims 30 and 39. In addition, as discussed above, Mollison does not disclose rapamycin as a "compound of the invention" useful for treating the diseases listed in Mollison, including any that are angiogenesis-mediated or a condition of the retina or choroid. Thus, based on the same reasoning as the Federal Circuit in *Ecolochem*, Applicants respectfully submit that Claims 68-74 are not anticipated for this additional reason. Finally, as discussed above respect to Claims 52-56 and 64-67, Mollison fails to disclose the specific ocular administration techniques recited in dependent Claims 71-74. For this additional reason, Claims 71-74 are not anticipated by Mollison.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

By the foregoing amendments and remarks, the Applicants respectfully submit that they have overcome the Examiner's rejections and request a timely issuance of a Notice of Allowance. If there are any remaining issues that can be resolved via telephone conversation, the Examiner is invited to call the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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